Figure 1

SEQUENCE LISTING

<110> WARNER-LAMBERT

<120> Matrix metalloproteinase inhibitors

<130> A0000434

<140>
<141>

<160> 1

<170> PatentIn Ver. 2.1

<210> 1
<211> 471
<212> PRT
<213> Homo sapiens

<400> 1

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Met His Pro Gly Val Leu Ala Ala Phe Leu Phe Leu Ser Trp Thr His
 1               5                  10                  15

Cys Arg Ala Leu Pro Leu Pro Ser Gly Gly Asp Glu Asp Asp Leu Ser
            20                  25                  30

Glu Glu Asp Leu Gln Phe Ala Glu Arg Tyr Leu Arg Ser Tyr Tyr His
        35                  40                  45

Pro Thr Asn Leu Ala Gly Ile Leu Lys Glu Asn Ala Ala Ser Ser Met
    50                  55                  60

Thr Glu Arg Leu Arg Glu Met Gln Ser Phe Phe Gly Leu Glu Val Thr
65                  70                  75                  80

Gly Lys Leu Asp Asp Asn Thr Leu Asp Val Met Lys Lys Pro Arg Cys
                85                  90                  95

Gly Val Pro Asp Val Gly Glu Tyr Asn Val Phe Pro Arg Thr Leu Lys
            100                 105                 110

Trp Ser Lys Met Asn Leu Thr Tyr Arg Ile Val Asn Tyr Thr Pro Asp
        115                 120                 125

Met Thr His Ser Glu Val Glu Lys Ala Phe Lys Lys Ala Phe Lys Val
    130                 135                 140

Trp Ser Asp Val Thr Pro Leu Asn Phe Thr Arg Leu His Asp Gly Ile
145                 150                 155                 160

Ala Asp Ile Met Ile Ser Phe Gly Ile Lys Glu His Gly Asp Phe Tyr
                165                 170                 175

Pro Phe Asp Gly Pro Ser Gly Leu Leu Ala His Ala Phe Pro Pro Gly
            180                 185                 190
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Pro Asn Tyr Gly Gly Asp Ala His Phe Asp Asp Asp Glu Thr Trp Thr
        195                 200                 205

Ser Ser Ser Lys Gly Tyr Asn Leu Phe Leu Val Ala Ala His Glu Phe
    210                 215                 220

Gly His Ser Leu Gly Leu Asp His Ser Lys Asp Pro Gly Ala Leu Met
225                 230                 235                 240

Phe Pro Ile Tyr Thr Tyr Thr Gly Lys Ser His Phe Met Leu Pro Asp
                245                 250                 255

Asp Asp Val Gln Gly Ile Gln Ser Leu Tyr Gly Pro Gly Asp Glu Asp
            260                 265                 270

Pro Asn Pro Lys His Pro Lys Thr Pro Asp Lys Cys Asp Pro Ser Leu
        275                 280                 285

Ser Leu Asp Ala Ile Thr Ser Leu Arg Gly Glu Thr Met Ile Phe Lys
    290                 295                 300

Asp Arg Phe Phe Trp Arg Leu His Pro Gln Gln Val Asp Ala Glu Leu
305                 310                 315                 320

Phe Leu Thr Lys Ser Phe Trp Pro Glu Leu Pro Asn Arg Ile Asp Ala
                325                 330                 335

Ala Tyr Glu His Pro Ser His Asp Leu Ile Phe Ile Phe Arg Gly Arg
            340                 345                 350

Lys Phe Trp Ala Leu Asn Gly Tyr Asp Ile Leu Glu Gly Tyr Pro Lys
        355                 360                 365

Lys Ile Ser Glu Leu Gly Leu Pro Lys Glu Val Lys Lys Ile Ser Ala
    370                 375                 380

Ala Val His Phe Glu Asp Thr Gly Lys Thr Leu Leu Phe Ser Gly Asn
385                 390                 395                 400

Gln Val Trp Arg Tyr Asp Asp Thr Asn His Ile Met Asp Lys Asp Tyr
                405                 410                 415

Pro Arg Leu Ile Glu Glu Asp Phe Pro Gly Ile Gly Asp Lys Val Asp
            420                 425                 430

Ala Val Tyr Glu Lys Asn Gly Tyr Ile Tyr Phe Phe Asn Gly Pro Ile
        435                 440                 445

Gln Phe Glu Tyr Ser Ile Trp Ser Asn Arg Ile Val Arg Val Met Pro
    450                 455                 460

Ala Asn Ser Ile Leu Trp Cys
465                 470
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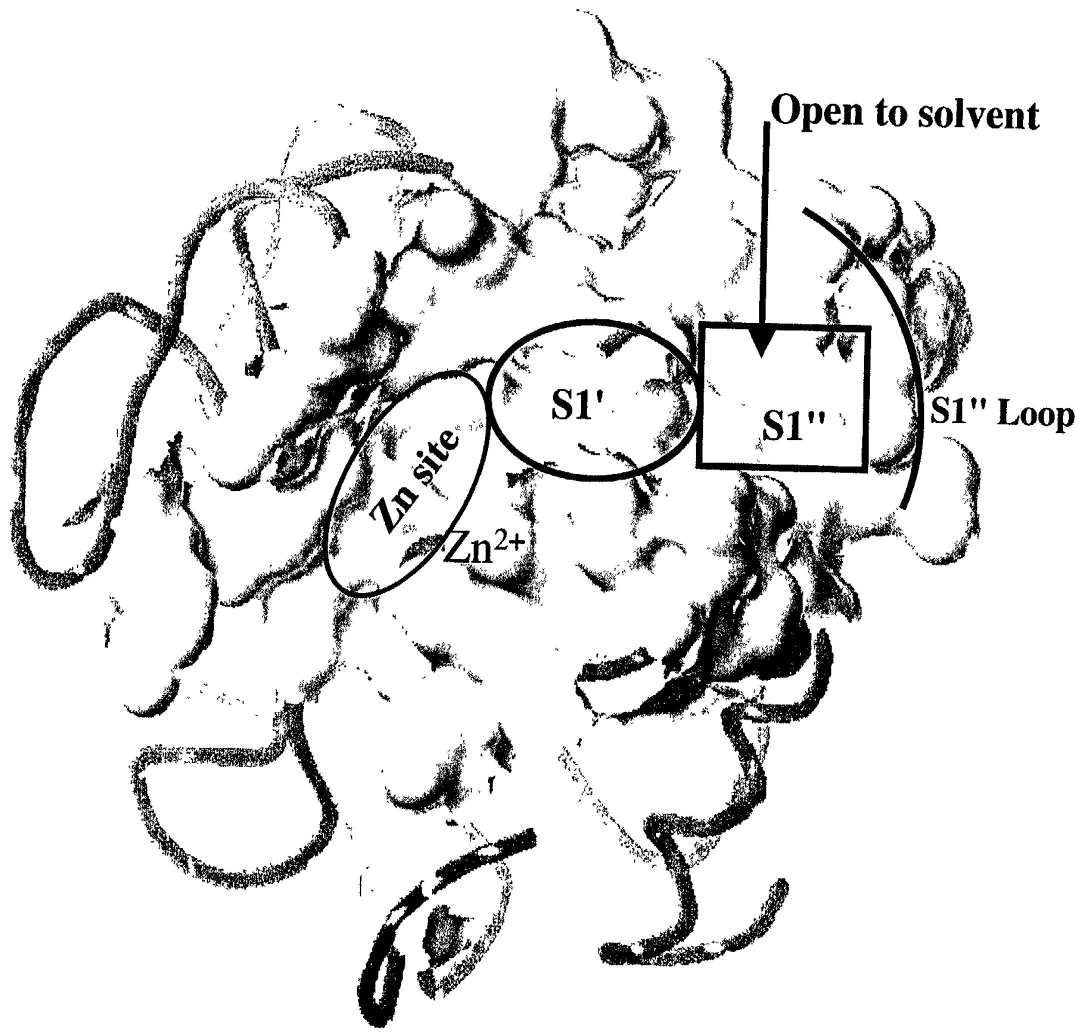
Figure 2



<u>Figure 3:</u> Synthesis example 1 binding mode

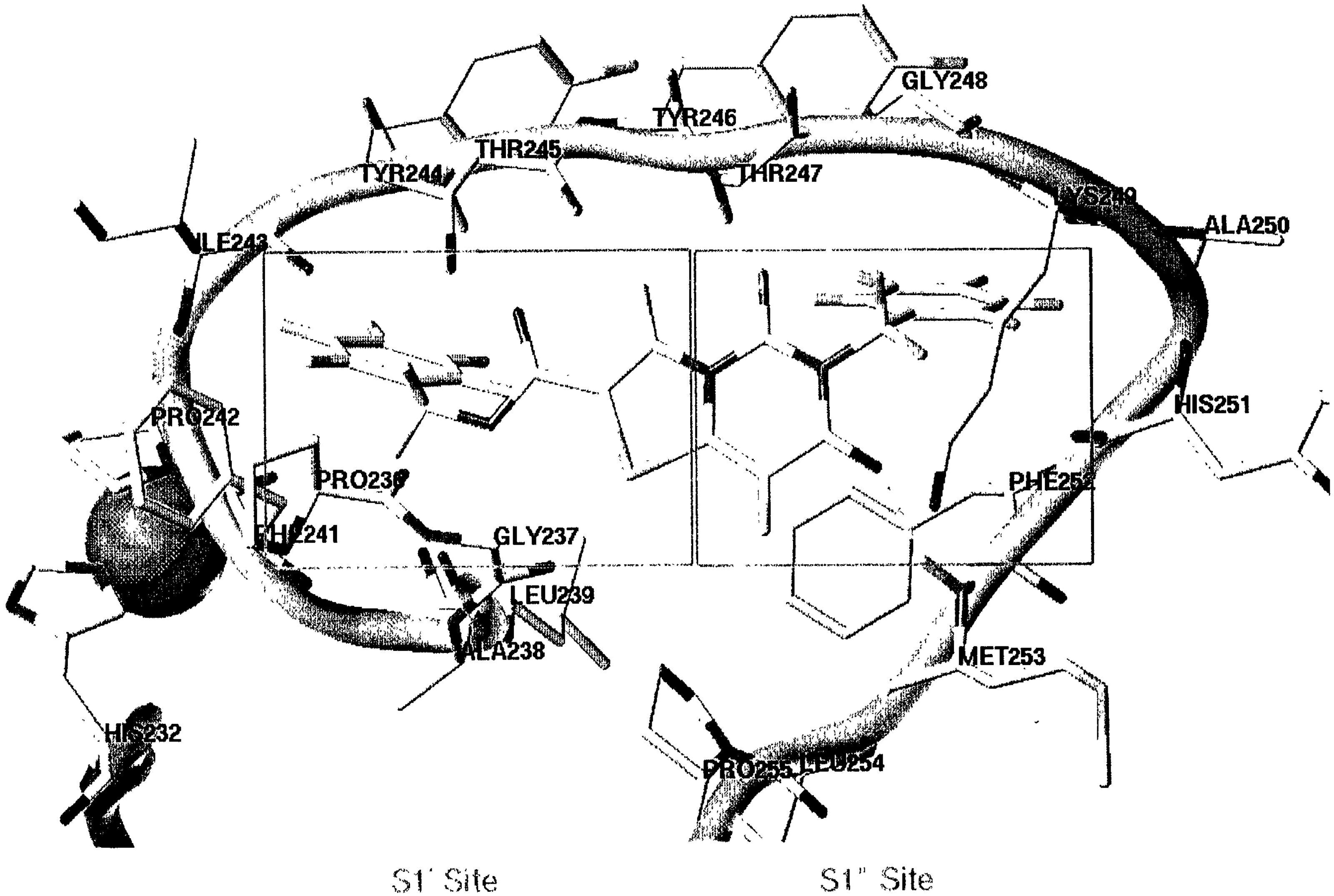
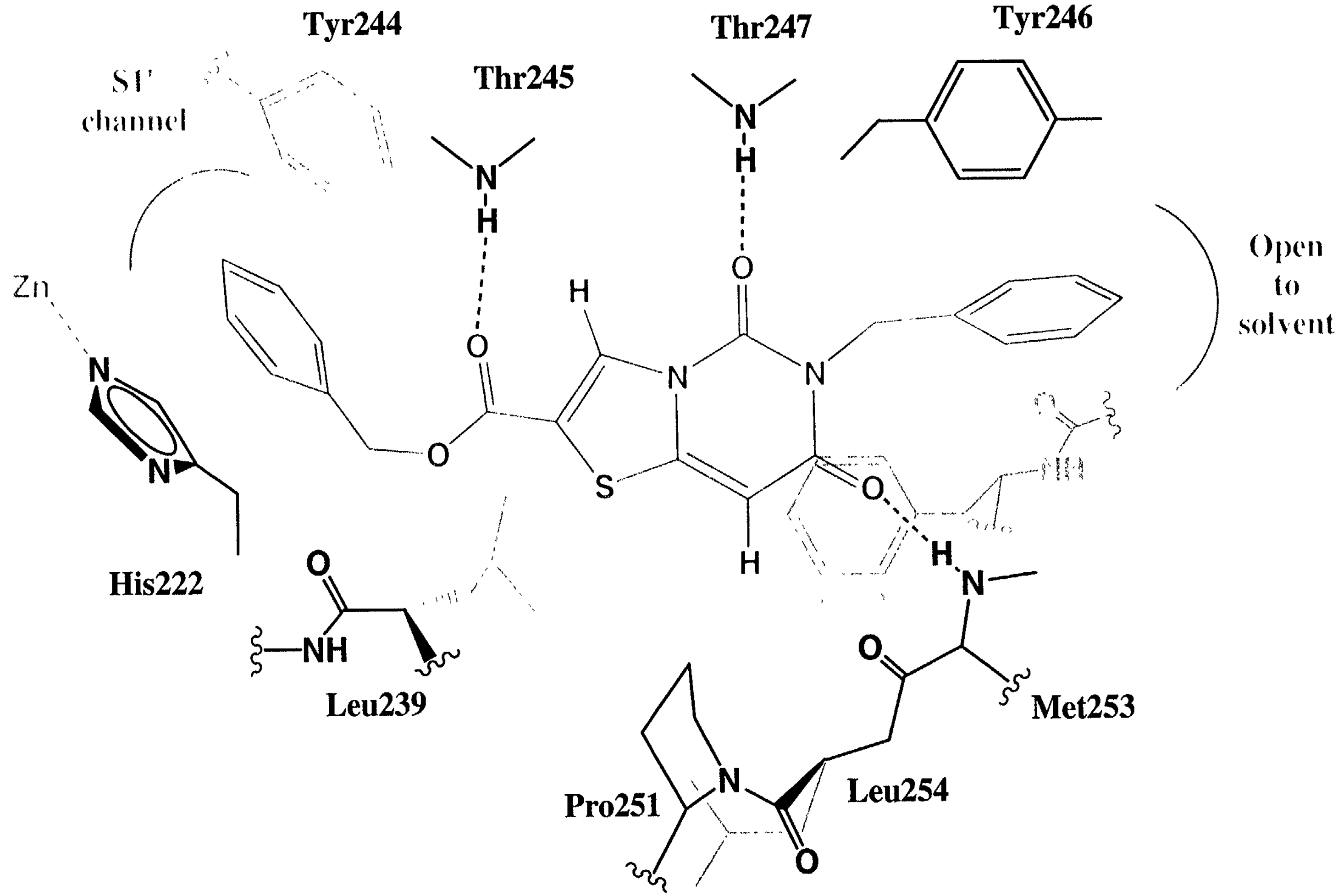


Figure 4: Synthesis example 1 binding mode



<u>Figure 5:</u> Synthesis example 10 binding mode

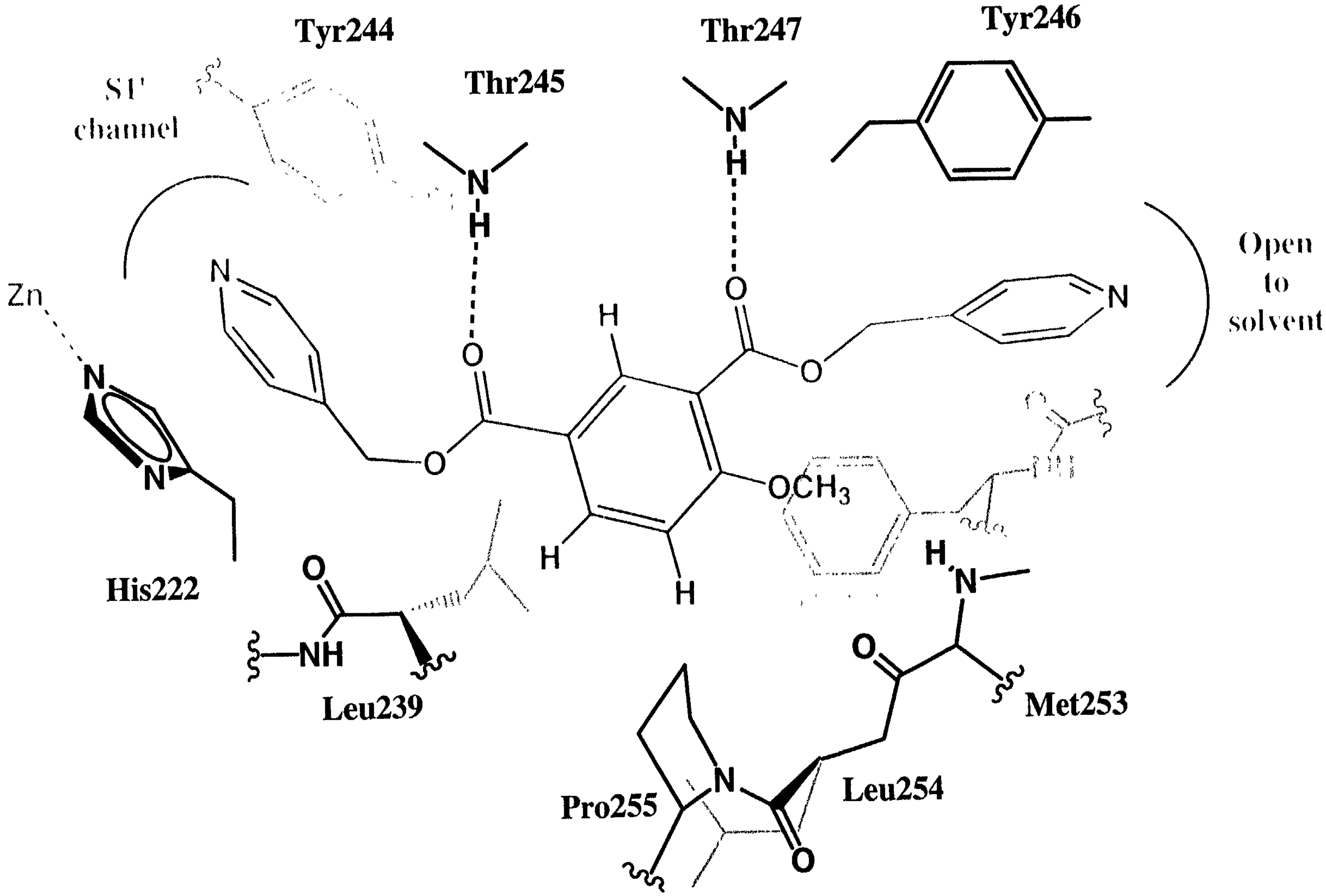


Figure 6: fused Bicyclic Pyrimidones-binding mode

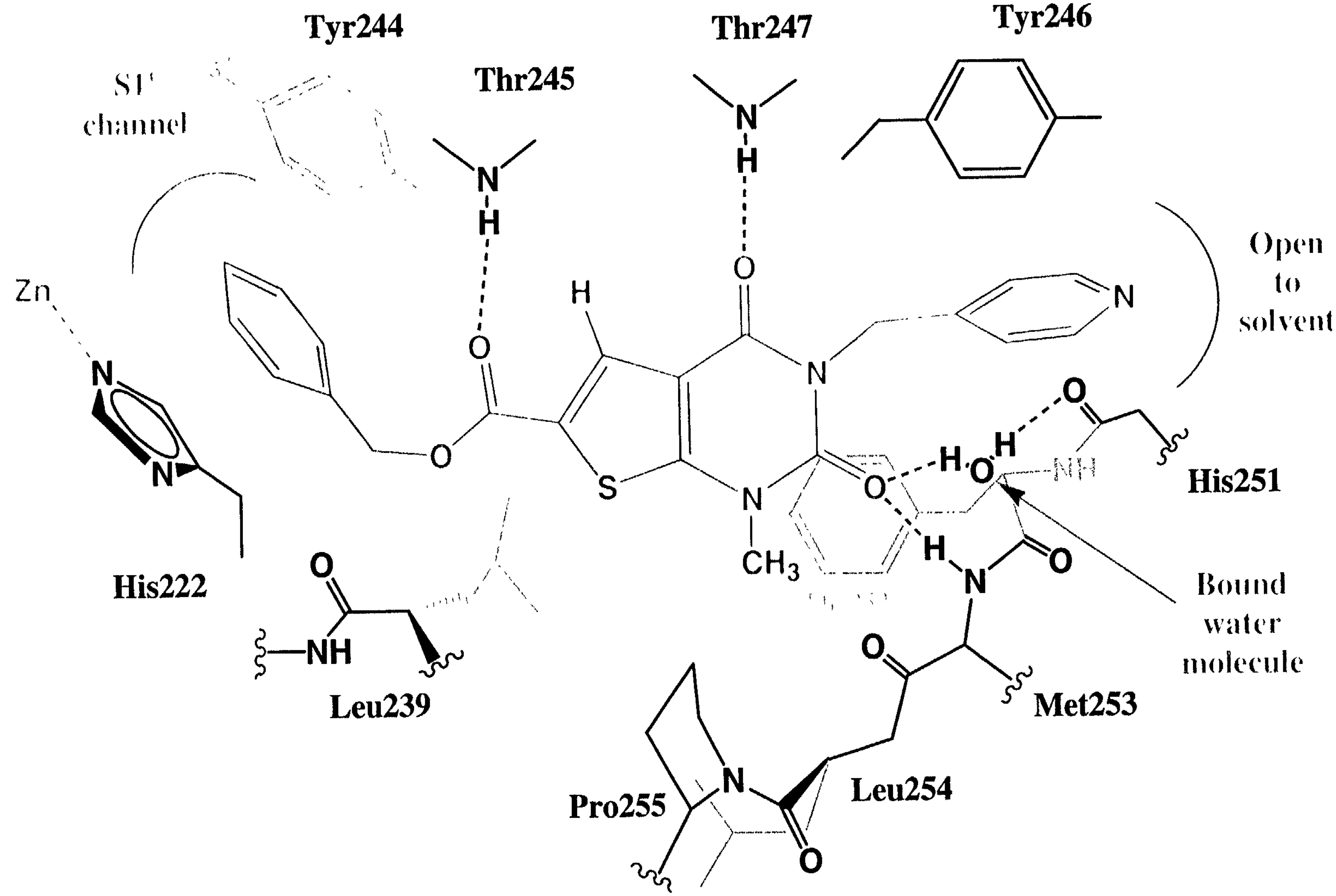


Figure 7: **Synthesis example 39 binding mode**

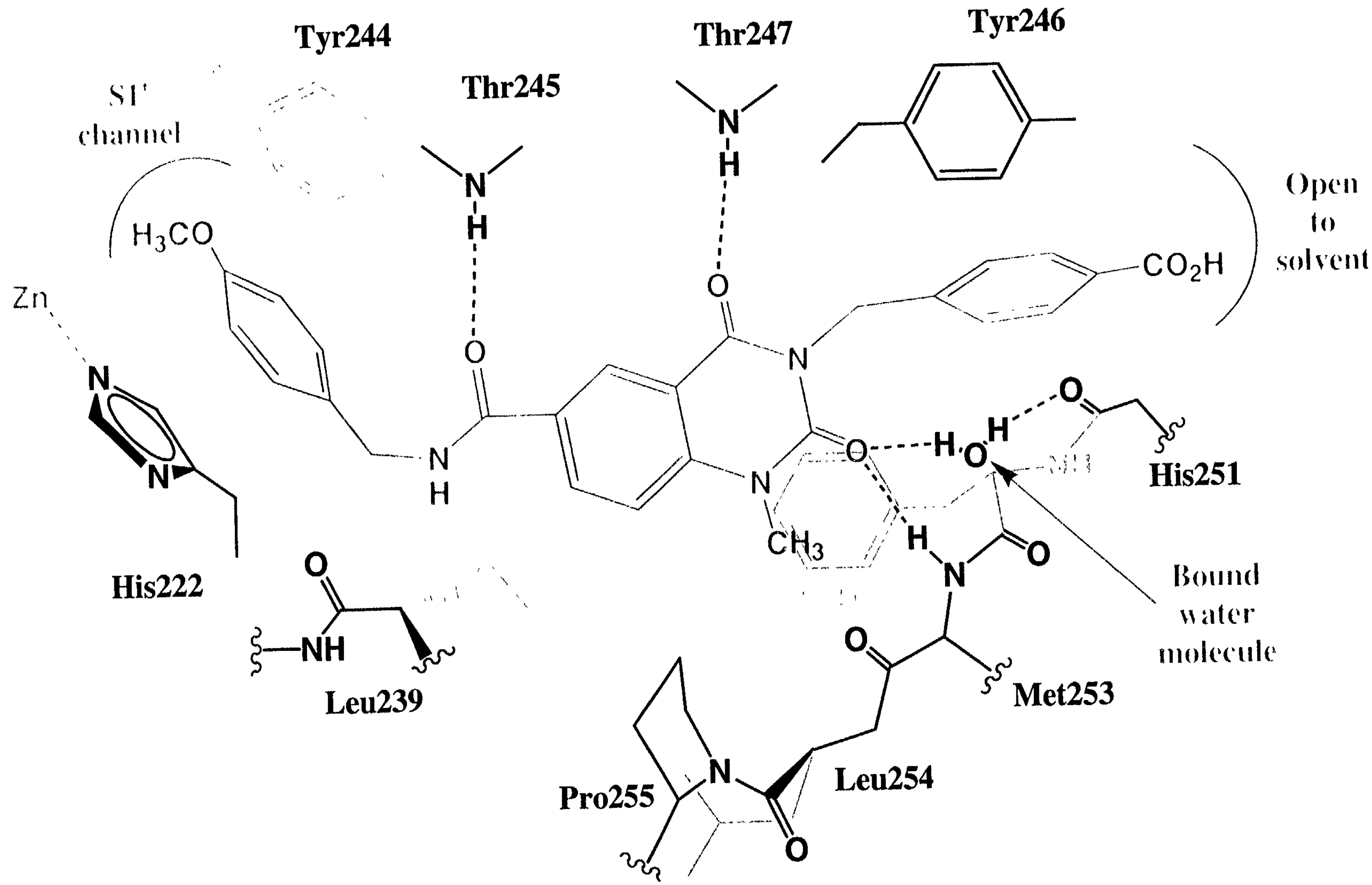


Figure 8: Synthesis example 57 binding mode

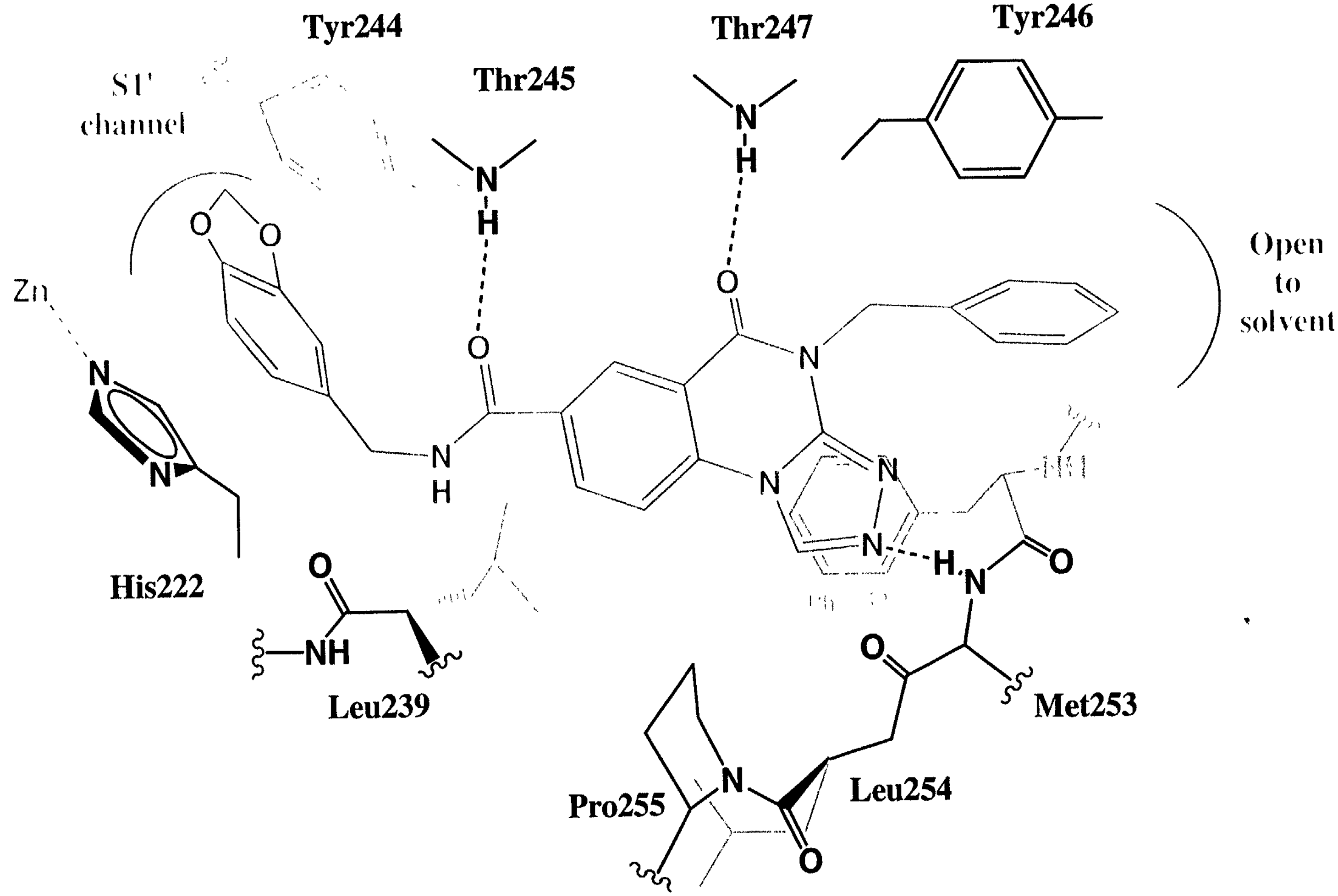


Figure 9 : **Coordonates in the space of the hydrophobic groups and hydrogen bond acceptors of the pharmacophore**